

CLAIMS

1. Use of anti-idiotypic vascular endothelial growth factor antibodies for the preparation of a medicament for treatment of pathologies involving endothelial cells engaged 5 in an angiogenesis process, either to inhibit the angiogenesis or to promote the angiogenesis, without affecting quiescent endothelial cells, or for the preparation of a product for diagnosis of pathologies involving endothelial cells engaged in an angiogenesis process.

2. Use of anti-idiotypic vascular endothelial growth factor antibodies for the 10 preparation of a medicament for treatment of pathologies involving angiogenic endothelial cells by selective stimulation of the KDR receptor.

3. Use of anti-idiotypic vascular endothelial growth factor antibodies according to one of claims 1 or 2 for the preparation of a medicament for treatment of pathologies 15 involving endothelial cells engaged in an angiogenesis process, to inhibit the angiogenesis, without affecting quiescent endothelial cells, which anti-idiotypic antibody is coupled to a toxin, the function of which is to block translation of proteins, or which anti-idiotypic antibody is in the form of an Fab fragment.

20 4. Use of anti-idiotypic vascular endothelial growth factor antibodies according to one of claims 1 or 2 for the preparation of a medicament for treatment of pathologies involving endothelial cells engaged in an angiogenesis process, to promote the angiogenesis, without affecting quiescent endothelial cells.

25 5. Use of anti-idiotypic vascular endothelial growth factor antibodies according to claim 3, in which the antibody is coupled to a toxin chosen from saporin and ricin or a radioactive element, such as iodine-125 or -131.

6. Use of anti-idiotypic antibodies for the preparation of a medicament for 30 treatment for stimulation of physiological angiogenesis, to increase the speed of formation of blood vessels in the course of cicatrization or maturation of the corpus luteum of the ovary, or

for stimulation of angiogenesis in the course of obstructive pathologies of vessels, in order to reperfuse regions rendered ischaemic during vascular thrombosis..

7. Use of anti-idiotypic antibodies associated with a toxin or of the Fab fragment of anti-idiotypic antibodies for the preparation of a medicament for treatment of pathologies requiring inhibition of angiogenesis, such as cancer, diabetic retinopathies and rejection of corneal grafts.

8. Use of anti-idiotypic vascular endothelial growth factor antibodies according to claim 1 for the preparation of a product for diagnosis of pathologies involving endothelial cells engaged in an angiogenesis process.

9. Anti-idiotypic vascular endothelial growth factor antibody, characterized in that it is a ligand of the human KDR receptor or of the murine flk-1 receptor and in that it is not a ligand of flt.

10. Anti-idiotypic vascular endothelial growth factor antibody, characterized in that it has the following properties:

- it is specific to KDR,
- it is circulating,
- it has a half-life of about 23 days, especially about 21 days, and in particular 22.5 days,
- it induces phosphorylation on a tyrosine of a protein of 200 kDa,
- it induces proliferation of vascular endothelial cells,
- it does not induce migration of endothelial cells,
- it stimulates angiogenesis,
- it does not cause arterial hypotension,
- it does not affect the permeability of vessels.

11. Fab fragment of the anti-idiotypic antibody according to claim 9.

12. Complex between an anti-idiotypic antibody according to claim 9 and a toxin, in particular chosen from saporin and ricin, or between an anti-idiotypic antibody according to claim 9 and a radioactive element, such as iodine-125 or -131.

5 13. Anti-idiotypic antibody according to claim 9 which can be obtained by the following process:

- purified VEGF is injected into an animal, in particular a rabbit,
- blood is withdrawn to recover purified Ig containing specific anti-VEGF IgG, for example by affinity chromatography for protein A, and then in a possible stage the specific
- 10 anti-VEGF IgG are purified from the purified Ig, for example by affinity chromatography for VEGF,
- the abovementioned purified Ig or the abovementioned purified anti-VEGF IgG are injected into an animal of the same species as that used for injection of the VEGF, in particular into the popliteal ganglions of a rabbit of the same origin as that used for injection
- 15 of the VEGF,
- blood is withdrawn to recover the total Ig, for example by protein A, and then to subject the total Ig to two immunoadsorptions:
 - . an immunoadsorption on an affinity column prepared with the pre-immune Ig of the rabbit which has been used to produce the anti-VEGF IgG, to eliminate
 - 20 the anti-allotypic or isotypic antibodies,
 - . an immunoadsorption on an affinity column prepared with the anti-VEGF IgG, to purify the anti-idiotypes.

14. Process for the preparation of an anti-idiotypic antibody according to claim 9, 25 characterized in that:

- purified VEGF is injected into an animal, in particular a rabbit,
- blood is withdrawn to recover purified Ig containing specific anti-VEGF IgG, for example by affinity chromatography for protein A, and then in a possible stage the specific anti-VEGF IgG are purified from the purified Ig, for example by affinity chromatography for
- 30 VEGF,
- the abovementioned purified Ig or the abovementioned purified anti-VEGF IgG are injected into an animal of the same species as that used for injection of the VEGF, in

particular into the popliteal ganglions of a rabbit of the same origin as that used for injection of the VEGF,

- blood is withdrawn to recover the total Ig, for example by protein A, and then to subject the total Ig to two immunoadsorptions:

- 5 . an immunoadsorption on an affinity column prepared with the pre-immune Ig of the rabbit which has been used to produce the anti-VEGF IgG, to eliminate the anti-allotypic or isotypic antibodies,
- . an immunoadsorption on an affinity column prepared with the anti-VEGF IgG, to purify the anti-idiotypes.

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15. Pharmaceutical compositions, characterized in that they comprise, as the active substance, an anti-idiotypic antibody according to claim 9 or 10, or the Fab fragment according to claim 11, or the complex according to claim 12.